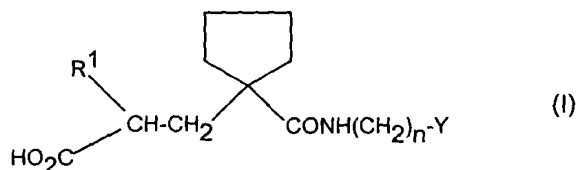


Claims

- 1 A method of treating female sexual dysfunction comprising administering a therapeutically effective amount of a compound of formula (I), pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof:



wherein

R^1 is C_{1-6} alkyl which may be substituted by one or more substituents, which may be the same or different, selected from the list: halo, hydroxy, C_{1-6} alkoxy, C_{2-6} hydroxyalkoxy, C_{1-6} alkoxy(C_{1-6} alkoxy), C_{3-7} cycloalkyl, C_{3-7} cycloalkenyl, aryl, aryloxy, (C_{1-4} alkoxy)aryloxy, heterocyclyl, heterocyclyloxy, $-NR^2R^3$, $-NR^4COR^5$, $-NR^4SO_2R^5$, $-CONR^2R^3$, $-S(O)_pR^6$, $-COR^7$ and $-CO_2(C_{1-4}$ alkyl); or R^1 is C_{3-7} cycloalkyl, aryl or heterocyclyl, each of which may be substituted by one or more substituents from said list, which substituents may be the same or different, which list further includes C_{1-6} alkyl; or R^1 is C_{1-6} alkoxy, $-NR^2R^3$ or $-NR^4SO_2R^5$;

wherein

R^2 and R^3 are each independently H, C_{1-4} alkyl, C_{3-7} cycloalkyl (optionally substituted by hydroxy or C_{1-4} alkoxy), aryl, (C_{1-4} alkyl)aryl, C_{1-6} alkoxyaryl or heterocyclyl; or R^2 and R^3 together with the nitrogen to which they are attached form a pyrrolidinyl, piperidino, morpholino, piperazinyl or N -(C_{1-4} alkyl)piperazinyl group;

R^4 is H or C_{1-4} alkyl;

R^5 is C_{1-4} alkyl, CF_3 , aryl, (C_{1-4} alkyl)aryl, (C_{1-4} alkoxy)aryl, heterocyclyl, C_{1-4} alkoxy or $-NR^2R^3$ wherein R^2 and R^3 are as previously defined;

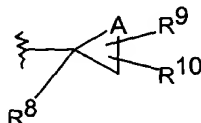
R^6 is C_{1-4} alkyl, aryl, heterocyclyl or NR^2R^3 wherein R^2 and R^3 are as previously defined; and

R^7 is C_{1-4} alkyl, C_{3-7} cycloalkyl, aryl or heterocyclyl; p is 0, 1, 2 or 3;

n is 0, 1 or 2;

the $-(CH_2)_n-$ linkage is optionally substituted by C_{1-4} alkyl, C_{1-4} alkyl substituted with one or more fluoro groups or phenyl, C_{1-4} alkoxy, hydroxy, hydroxy(C_{1-3} alkyl), C_{3-7} cycloalkyl, aryl or heterocyclyl;

Y is the group



wherein A is $-(CH_2)_q-$ where q is 1, 2, 3 or 4 to complete a 3 to 7 membered

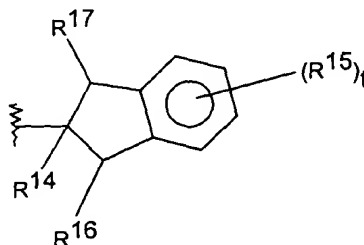
carbocyclic ring which may be saturated or unsaturated; R^8 is H, C_{1-6} alkyl, $-CH_2OH$, phenyl, phenyl(C_{1-4} alkyl) or $CONR^{11}R^{12}$; R^9 and R^{10}

are each independently H, $-CH_2OH$, $-C(O)NR^{11}R^{12}$, C_{1-6} alkyl, phenyl (optionally substituted by C_{1-4} alkyl, halo or C_{1-4} alkoxy or phenyl(C_{1-4} alkyl) wherein the phenyl group is optionally substituted by C_{1-4} alkyl, halo or C_{1-4} alkoxy, or R^9 and R^{10} together form a dioxolane; R^{11} and

R^{12} which may be the same or different are H, C_{1-4} alkyl, R^{13} or $S(O)_rR^{13}$, where r is 0, 1 or 2 and R^{13} is phenyl optionally substituted by C_{1-4} alkyl or phenyl(C_{1-4} alkyl) wherein the phenyl is optionally substituted by C_{1-4} alkyl; or

Y is the group, $-C(O)NR^{11}R^{12}$ wherein R^{11} and R^{12} are as previously defined except that R^{11} and R^{12} are not both H; or

Y is the group,

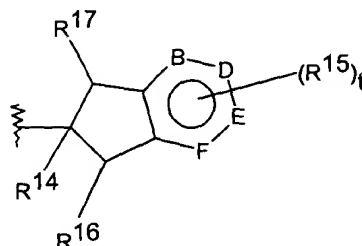


wherein R^{14} is H, CH_2OH , or $C(O)NR^{11}R^{12}$ wherein R^{11} and R^{12} are as

previously defined; when present R^{15} , which may be the same or different

to any other R^{15} , is OH, C_{1-4} alkyl, C_{1-4} alkoxy, halo or CF_3 ; t is 0, 1, 2, 3 or 4; and R^{16} and R^{17} are independently H or C_{1-4} alkyl; or

Y is the group



5 wherein one or two of B, D, E or F is a nitrogen, the others being carbon; and R^{14} to R^{17} and t are as previously defined; or

Y is an optionally substituted 5-7 membered heterocyclic ring, which may be saturated, unsaturated or aromatic and contains a nitrogen, oxygen or sulphur and optionally one, two or three further nitrogen atoms in the ring and which may be optionally benzofused and optionally substituted by:

10 C_{1-6} alkoxy; hydroxy; oxo; amino; mono or di- $(C_{1-4}$ alkyl)amino;

C_{1-4} alkanoylamino; or

C_{1-6} alkyl which may be substituted by one or more substituents, which may be the same or different, selected from the list: C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{1-6} alkylthio, halogen, C_{3-7} cycloalkyl, heterocyclyl or phenyl; or

15 C_{3-7} cycloalkyl, aryl or heterocyclyl, each of which may be substituted by one or more substituents, which may be the same or different, selected from the list: C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{1-6} alkylthio, halogen, C_{3-7} cycloalkyl, heterocyclyl or phenyl;

20 wherein when there is an oxo substitution on the heterocyclic ring, the ring only contains one or two nitrogen atoms and the oxo substitution is adjacent a nitrogen atom in the ring; or

Y is $-NR^{18}S(O)_uR^{19}$, wherein R^{18} is H or C_{1-4} alkyl; R^{19} is aryl, aryl C_{1-4} alkyl or heterocyclyl; and u is 0, 1, 2 or 3.

25

2 A compound of formula (I), pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein R^1 , n and Y are as defined in claim 1 with the proviso that Y is not the group $-C(O)NR^{11}R^{12}$ and when R^1 is propyl or phenylethyl, R^{14} is not $-CH_2OH$.

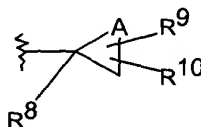
3 A compound of formula (I), pharmaceutically acceptable salts, solvates,
polymorphs or prodrugs thereof, wherein R^1 , n and Y are as defined in claim 1
with the proviso that Y is not the group $-C(O)NR^{11}R^{12}$ and R^{14} is not H or
5 $-CH_2OH$.

4 A compound according to claim 2, pharmaceutically acceptable salts, solvates,
polymorphs or prodrugs thereof, wherein R^1 is C_{1-6} alkyl, C_{1-6} alkoxy,
10 C_{1-6} alkoxy(C_{1-3})alkyl, C_{1-6} alkoxy C_{1-6} alkoxy C_{1-3} alkyl or C_{1-6} alkyl substituted
with aryl.

5 A compound according to claim 4, pharmaceutically acceptable salts, solvates,
15 polymorphs or prodrugs thereof, wherein R^1 is C_{1-6} alkyl, C_{1-6} alkoxy,
 C_{1-6} alkoxy(C_{1-3})alkyl or C_{1-6} alkoxy C_{1-6} alkoxy C_{1-3} alkyl.

6 A compound according to claim 5, pharmaceutically acceptable salts, solvates,
polymorphs or prodrugs thereof, wherein R^1 is C_{1-4} alkyl or
20 C_{1-6} alkoxy(C_{1-3})alkyl.

7 A compound according to claim 2, pharmaceutically acceptable salts, solvates,
polymorphs or prodrugs thereof, wherein when Y is the group



25 and the carbocyclic ring is fully saturated, then preferably one of R^9 or R^{10} is
 $-CH_2OH$; $-C(O)NR^{11}R^{12}$; C_{1-6} alkyl; phenyl optionally substituted by C_{1-4} alkyl;
or phenyl(C_{1-4} alkyl) wherein the phenyl group is optionally substituted by
 C_{1-4} alkyl.

30 8 A compound according to claim 7, pharmaceutically acceptable salts, solvates,
polymorphs or prodrugs thereof, wherein the carbocyclic ring is 5, 6 or 7

membered wherein one of R⁹ or R¹⁰, is -C(O)NR¹¹R¹², with the other being C₁-₆alkyl; phenyl optionally substituted by C₁-₄alkyl; or phenyl(C₁-₄alkyl) wherein the phenyl group is optionally substituted by C₁-₄alkyl.

- 5 9 A compound according to claim 7 , pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein R⁹ and R¹⁰ are attached to adjacent carbon atoms in the ring.
- 10 10 A compound according to claim 7 pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein R⁸ is CH₂OH.
- 15 11 A compound according to claim 2 , pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein when Y is the group -NR¹⁸S(O)_uR¹⁹, preferably R¹⁸ is H.
- 20 12 A compound according to claim 2 , pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein R¹⁹ is benzyl or phenyl.
- 25 13 A compound according to claim 2, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein u is 2.
- 30 14 A compound according to claim 2, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein Y is an optionally substituted 5-7 membered heterocyclic ring.
- 35 15 A compound according to claim 14, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein the 5-7 membered heterocyclic ring is an optionally substituted aromatic ring.
- 35 16 A compound according to claim 15, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein said aromatic ring is pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, pyrazolyl, triazolyl, tetrazolyl, oxadiazolyl, thiazolyl, thiadiazolyl, oxazolyl, isoxazolyl, indolyl, isoindolyl, quinolyl, isoquinolyl, pyridonyl, quinoxalyl or quinazolinyl each of which may be substituted as defined in claim 1.

- 17 A compound according to claim 16, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein the aromatic ring is oxadiazole, pyridone or thiadiazole each of which may be substituted as defined in claim 1.

5

- 18 A compound according to claim 17, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein the aromatic ring is 1,2,5-oxadiazole, 1,3,4-oxadiazole, 2-pyridone or 1,3,4-thiadiazole each of which may be substituted as defined in claim 1.

10

- 19 A compound according to claim 14, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein the 5-7 membered heterocyclic ring is substituted by one or more C₁₋₆alkyl, phenyl or phenylC₁₋₄alkyl.

15

- 20 A compound according to claim 19, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein the 5-7 membered heterocyclic ring is substituted by C₁₋₄alkyl or benzyl.

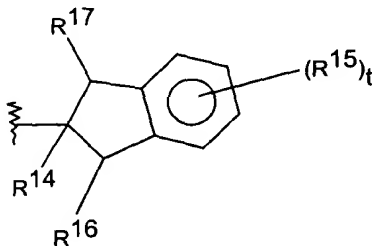
20

- 21 A compound according to claim 17, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein when Y is a pyridone said pyridone is *N*-substituted pyridone.

- 22 A compound according to claim 14, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein Y is a lactam linked at the nitrogen.

25

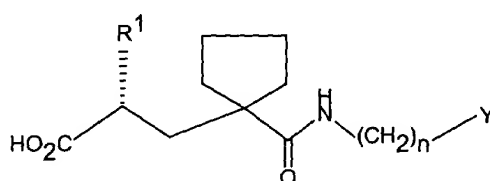
- 23 A compound according to any claim 2, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein Y is



30

wherein R¹⁴ is CH₂OH or C(O)NR¹¹R¹²

- 24 A compound according to claim 2, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein R¹⁶ and R¹⁷ are hydrogen.
- 25 A compound according to claim 2, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, wherein t is 0.
- 26 A compound of formula Ie, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof,



(Ie)

wherein R¹, Y and n are as defined in claim 2.

- 27 A compound, pharmaceutically acceptable salts, solvates, polymorphs or prodrugs thereof, selected from the group consisting of:
- 2-[(1-[(1-benzyl-6-oxo-1,6-dihydro-3-pyridinyl)amino]carbonyl)cyclopentyl]-methyl]-4-methoxybutanoic acid;
- 2-[(1-[(3-(2-oxo-1-pyrrolidinyl)propyl)amino]carbonyl)cyclopentyl]-methyl]-4-phenylbutanoic acid;
- (+)-2-[(1-[(2-(hydroxymethyl)-2,3-dihydro-1H-inden-2-yl)amino]carbonyl)cyclopentyl]-methyl]-4-phenylbutanoic acid;
- 2-[(1-[(5-methyl-1,3,4-thiadiazol-2-yl)amino]carbonyl)cyclopentyl]-methyl]-4-phenylbutanoic acid;
- cis-3-(2-methoxyethoxy)-2-[(1-[(4-[(phenylsulfonyl)amino]carbonyl)cyclohexyl]-amino]carbonyl)cyclopentyl]-methyl]propanoic acid;
- (+)-2-[(1-[(2-(hydroxymethyl)-2,3-dihydro-1H-inden-2-yl)amino]carbonyl)cyclopentyl]-methyl]pentanoic acid;
- (2R)-2-[(1-[(5-ethyl-1,3,4-thiadiazol-2-yl)amino]carbonyl)cyclopentyl]-methyl]pentanoic acid or (-)-2-[(1-[(5-ethyl-1,3,4-thiadiazol-2-yl)amino]carbonyl)cyclopentyl]-methyl]pentanoic acid;
- (2S)-2-[(1-[(5-ethyl-1,3,4-thiadiazol-2-yl)amino]carbonyl)cyclopentyl]-methyl]pentanoic acid or (+)-2-[(1-[(5-ethyl-1,3,4-thiadiazol-2-yl)amino]carbonyl)cyclopentyl]-methyl]pentanoic acid ;

- 2-({1-[(3-benzylanilino)carbonyl]cyclopentyl)methyl}pentanoic acid ;
2-[(1-[(1-benzyl-6-oxo-1,6-dihydro-3-pyridinyl)amino]carbonyl)cyclopentyl]-
methyl}pentanoic acid ;
2-[(1-[(1R,3S,4R)-4-(aminocarbonyl)-3-butylcyclohexyl]amino)carbonyl]-
5 cyclopentyl)methyl}pentanoic acid ;
trans-3-[1-([2-(4-chlorophenyl)cyclopropyl]amino)carbonyl]cyclopentyl]-2-
(methoxymethyl)propanoic acid ;
trans-3-[1-([2-(4-methoxyphenyl)cyclopropyl]amino)carbonyl]cyclopentyl]-2-
(methoxyethyl)propanoic acid ;
10 *trans*-3-[1-([2-pentylcyclopropyl]amino)carbonyl]cyclopentyl]-2-
(methoxyethyl)propanoic acid ;
3-[1-([5-benzyl-1,3,4-thiadiazol-2-yl]amino)carbonyl]cyclopentyl]-2-
(methoxyethyl)propanoic acid ;
3-[1-([4-butylpyridin-2-yl]amino)carbonyl]cyclopentyl]-2-(methoxyethyl)propanoic
15 acid ;
3-[1-([4-phenylpyridin-2-yl]amino)carbonyl]cyclopentyl]-2-
(methoxyethyl)propanoic acid ;
3-[1-([1-hydroxymethyl-3-phenylcyclopentyl]amino)carbonyl]cyclopentyl]-2-
(methoxyethyl)propanoic acid ;
20 2-[(1-([2-(hydroxymethyl)-2,3-dihydro-1*H*-inden-2-yl]amino)carbonyl)-
cyclopentyl)methyl]-4-methoxybutanoic acid ;
trans-3-[1-([2-phenylcyclopropyl]amino)carbonyl]cyclopentyl]-2-
(methoxyethyl)propanoic acid ;
(*R*)- 2-[(1-([2-(hydroxymethyl)-2,3-dihydro-1*H*-inden-2-yl]amino)carbonyl)-
25 cyclopentyl)methyl]-4-methoxybutanoic acid ; and
(*S*)-2-[(1-([2-(hydroxymethyl)-2,3-dihydro-1*H*-inden-2-yl]amino)carbonyl)-
cyclopentyl)methyl]-4-methoxybutanoic acid .

28 The method according to claim 1 wherein the female sexual dysfunction treated
30 includes at least female sexual arousal dysfunction (FSAD).

29 The method according to claim 1 wherein the medicament is administered
systemically.

35 30 The method according to claim 1 wherein the medicament is administered orally.

31 A method of treatment or prophylaxis of a condition for which a beneficial therapeutic response can be obtained by the inhibition of neutral endopeptidase comprising administration of a therapeutically effective amount of a compound as defined in claim 2.

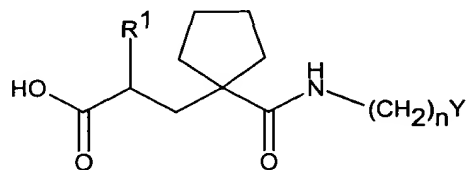
5 32 A medicine comprising the compound of claim 2.

33 A pharmaceutical formulation including a compound as defined in claim 2 together with a pharmaceutically acceptable excipient.

10 34 A method for the treatment or prophylaxis of female sexual dysfunction including administering to the patient a therapeutically effective amount of a compound as defined in claim 2.

15 35 A female sexual dysfunction pharmaceutical formulation including a therapeutically effective amount of a compound as defined in claim 2 together with a pharmaceutically acceptable excipient.

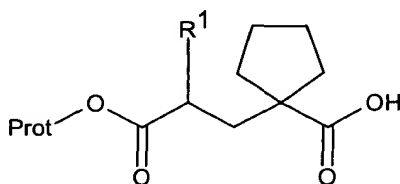
20 36 A process for preparing a compound of formula I or salts thereof



(I)

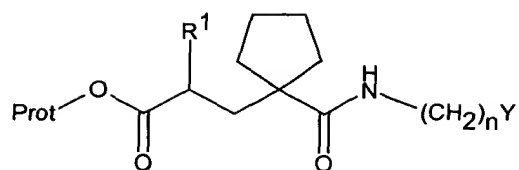
wherein R^1 , n and Y are as defined in any one of claims 2 to 27, comprising the steps of:

a) reacting a compound of formula II



(II)

25 wherein Prot is a suitable protecting group, with a compound of formula $Y(CH_2)_nNH_2$ (III), to give a compound of formula IV,



(IV)

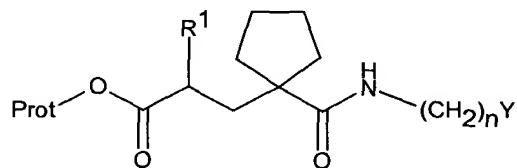
;

then

- b) reacting the compound of formula IV under suitable deprotecting conditions to give the compound of formula I; then
- c) optionally forming a salt.

5

37. A compound of formula IV



(IV)

,

10

wherein R¹, n, and Y are as defined in claim 2 and wherein Prot is a protecting group.